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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/938,112	08/23/2001	Stephen Donovan	D-2875DIV	1929

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 07/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/938,112	DONOVAN, STEPHEN	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21,22,36,37,67-75,77 and 78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *21,22,36,37,67,68, 70-72, 77 and 78* is/are allowed.

6)☒ Claim(s) *69 and 73-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 21, 22, 36, 37, 67-75, 77 and 78 are pending.

Applicants' amendment filed April 23, 2004 is acknowledged. Applicant's response has been fully considered. Claims 23-25, 76, 79 and 80 have been cancelled, thus claims 21, 22, 36, 37, 67-75, 77 and 78 are examined.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

2. The previous rejection of claim 76 under 35 U.S.C. 112, first paragraph, is withdrawn in view of applicant's cancellation of the claim and applicant's response at page 7 in the amendment filed April 23, 2004.

Claim Rejections - 35 USC § 102

3. The previous rejection of claims 23-25 and 79-80 under 35 U.S.C. 102(e) as being anticipated by Quinn *et al.* (U.S. Patent 6,632,440 B1), is withdrawn in view of applicant's cancellation of the claim and applicant's response at pages 7-8 in the amendment filed April 23, 2004.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 69, 73, 74 and 75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 69 is indefinite because the claim recites clostridial neurotoxin is produced by a clostridial organism, however, claim 67, which claim 69 is dependent from, indicates the clostridial neurotoxin is produced in a host cell (e.g., *E. coli*) by expression of the genetic construct, thus, it is not clear whether the neurotoxin is produced naturally by a clostridial organism or recombinantly by a host cell. See also claims 73, 74 and 75.

A proposed amendment to claims 21, 36, 37, 67, 69, 73-75, 77 and 78 is suggested.

21. (Currently amended) A method for obtaining an agent for alleviating pain, the method comprising:

(a) producing a genetic construct having nucleic acids encoding a clostridial neurotoxin;

(b) incorporating the construct into a host cell;

(c) culturing the cell under conditions sufficiently for expression of [expressing the construct to produce] the clostridial neurotoxin; and

(d) covalently attaching the clostridial neurotoxin to a targeting moiety which comprises substance P, wherein H_C has been removed from the clostridial neurotoxin or modified so as to reduce the ability of the clostridial neurotoxin to bind to a receptor for the H_C at a neuromuscular junction.

36. (Currently amended) A plasmid encoding a clostridial neurotoxin, comprising:

(a) a first nucleotide sequence [region] comprising;

(i) a first [portion] nucleotide segment encoding an amino acid sequence [region] comprising a targeting moiety [that comprises] of substance P [and is] able to specifically bind to receptors on cells under physiological conditions; and (ii) a second [portion] nucleotide segment encoding an

amino acid sequence [region] comprising a translocation element able to facilitate the transfer of a polypeptide across an endosome membrane; and

(b) a second nucleotide sequence [region] encoding an [additional] amino acid sequence [region] comprising a therapeutic element having an intracellular protease biological activity when released into the cytoplasm of a target cell, and an [origin of] element for replication directing plasmid replication by a host cell, wherein H_C has been removed from the clostridial neurotoxin or modified so as to reduce the ability of the clostridial neurotoxin to bind to a receptor for the H_C at a neuromuscular junction.

37. (Currently amended) A method of making a clostridial neurotoxin comprising:

(a) inserting the plasmid of claim 36 into a suitable host cell,

(b) [growing] culturing the host cell [in culture, and

(c) permitting the host cell] under conditions sufficient to express the [polypeptide from the plasmid.] clostridial neurotoxin; and

(d) isolating the clostridial neurotoxin.

67. (Currently amended) A method for obtaining an agent for alleviating pain, the method comprising:

(a) producing a genetic construct having nucleic acids encoding a clostridial neurotoxin;

(b) incorporating the construct into a host cell;

(c) culturing the cell under conditions sufficient for expression of [expressing the construct to produce] the clostridial neurotoxin; and

(d) covalently attaching the clostridial neurotoxin to substance P, wherein H_C has been removed from the clostridial neurotoxin or modified so as to reduce the ability of the clostridial neurotoxin to bind to a receptor for the H_C at a neuromuscular junction.

69. (Currently amended) The method of claim 67, wherein the clostridial neurotoxin is [produced by] a neurotoxin from an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum and Clostridial tetani.

73. (Currently amended) The method of claim 72, wherein the H_N is [produced by] a translocation domain of a clostridial neurotoxin from an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum and Clostridial tetani.

74. (Currently amended) The method of claim 72, wherein the L chain is [produced by] a light chain of a clostridial neurotoxin from an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum and Clostridial tetani.

75. (Currently amended) The method of claim 72, wherein the H_N is [obtained from] a translocation domain of a botulinum toxin selected from the group consisting of botulinum toxin serotype A, serotype B, serotype C1, serotype D, serotype E, serotype F, and serotype G.

77. (Currently amended) A method for obtaining an agent for alleviating pain, the method comprising:

(a) producing a genetic construct having nucleic acids encoding a botulinum toxin serotype A;

(b) incorporating the construct into a host cell;

(c) culturing the cell under conditions sufficient for expression of [expressing the construct to produce] the botulinum toxin serotype A; and

(d) covalently attaching the botulinum toxin serotype A to substance P, wherein H_C has been removed from the botulinum toxin or modified so as to reduce the ability of the botulinum toxin to bind to a receptor for the H_C at a neuromuscular junction.

78. (Currently amended) A method for obtaining an agent for alleviating pain, the method comprising:

(a) producing a genetic construct having nucleic acids encoding a botulinum toxin, wherein the [portion] nucleotide sequence encoding an H_C of the toxin has been removed;

(b) incorporating the construct into a host cell;

(c) culturing the cell under conditions sufficient for expression of [expressing the construct to produce] the botulinum toxin; and

(d) covalently attaching the botulinum toxin to substance P.

Conclusion

5. Claims 69, 73, 74 and 75 are rejected, it appears that claims 21, 22, 36, 37, 67, 68, 70-72, 77 and 78 are free of prior art and allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner

CMK
July 1, 2004

Jon P. Weber, Ph.D.
Primary Examiner